Journal of Nuclear Medicine, published on February 16, 2017 as doi:10.2967/jnumed.116.187138

Equivalent dose rate at 1m of patients with known or suspected neuroendocrine tumor exiting a nuclear medicine department after ^{68}Ga-DOTATOC, ^{18}F-FDOPA or ^{18}F-FDG PET/CT, or ^{111}In-pentetreotide or ^{123}I-mIBG SPECT/CT

Jules Zhang-Yin, Department of Nuclear Medicine, Hôpital Tenon, AP-HP, Paris, France/ Université Pierre et Marie Curie (UPMC), Paris, France.

Anne-Sophie Dirand, Department of Nuclear Medicine, Hôpital Tenon, AP-HP, Paris, France.

Myriam Sasanelli, Department of Nuclear Medicine, Hôpital Cochin, AP-HP, Paris, France.

Gwenaelle Corrégé, Department of Nuclear Medicine, Hôpital Tenon, AP-HP, Paris, France.

Aude Peudon, Department of Nuclear Medicine, Hôpital Cochin, AP-HP, Paris, France.

Thierry Kiffel, Université Pierre et Marie Curie (UPMC), Paris, France.

Valérie Nataf, Radiopharmacy, Hôpital Tenon, AP-HP, Paris

Jérôme Clerc, Department of Nuclear Medicine, Hôpital Cochin, AP-HP, Paris, France.

Françoise Montravers, Department of Nuclear Medicine, Hôpital Tenon, AP-HP, Paris, France/ Université Pierre et Marie Curie (UPMC), Paris, France.

Jean-Noël Talbot, Department of Nuclear Medicine, Hôpital Tenon, AP-HP, Paris, France/ Université Pierre et Marie Curie (UPMC), Paris, France.

There is no disclaimer.

Author responsible and first author:

Name: Jules Zhang-Yin (not in training)

Address: Department of Nuclear Medicine, Hôpital Tenon, 4 rue de Chine, 75020, Paris, France

Telephone number: 01.56.01.67.98 Fax 01.56.01.77.87

Email address: juleszhangyin@gmail.com

Word count of the manuscript: 3740

Disclosure: None

Financial support: None

Abstract

^{123}I-mIBG and ^{111}In-pentetrotide SPECT have been used for functional imaging of neuroendocrine tumors (NET) for the last two decades. More recently, PET/CT imaging with ^{18}F-FDG, ^{18}F-FDOPA and ^{68}Ga somatostatin-receptor ligands in NETs has been expanding. No direct measurements of the dose rate from NET patients exiting the nuclear medicine department could be found in the literature after PET/CT with ^{18}F-FDOPA or ^{68}Ga-DOTATOC, a somatostatin analogue.

Methods: We measured the dose rates from NET patients undergoing PET/CT or SPECT/CT in our centers. A total of 103 paired measurements of equivalent dose rate at 1m of the patient (EDR-1m) were performed in 98 patients on leaving the department. The detector was facing the sternum or the urinary bladder, at a distance of 1 meter from and right in front of the patient. The practice for exiting the department differed according to whether the patient was referred to PET/CT or to SPECT/CT. PET/CT patients were discharged after imaging.

Results: The median administered activity was 122 MBq in 53 ^{68}Ga-DOTATOC PET/CTs, 198 MBq in 15 ^{18}F-FDOPA PET/CTs and 176 MBq in 13 ^{18}F-FDG PET/CTs. The corresponding median EDR-1m (in µSv/h) were 4.8, 9.5 and 8.8 respectively facing the sternum, and 5.1, 10.1 and 9.5 respectively facing the bladder.

SPECT/CT patients left the department earlier, just after radiopharmaceutical injection. The median administered activity was 170 MBq in 12 ^{111}In-pentetreotide SPECT/CTs and 186 MBq in 10 ^{123}I-mIBG SPECT/CTs. The corresponding median EDR-1m (in µSv/h) were 9.4, and 4.9 respectively at the level of the sternum, and 9.3 and 4.7 respectively at the level of the bladder. The EDR-1m was <20 µSv/h in all patients. Thus when exiting the nuclear medicine department, the NET patients injected with ^{68}Ga-DOTATOC or ^{123}I mIBG emitted an average EDR-1m roughly half of that of patients injected with other radiopharmaceuticals. This is a complementary argument for replacing SPECT by PET somatostatin-receptor imaging.

Conclusion: Our current practice of allowing patients to exit after PET/CT imaging or just after SPECT radiopharmaceutical injection appears to be safe from a radiation protection point of view. Restrictive advice is unnecessary for NET patients discharged from the department.

Key-words

radiation protection – dose rate – Somatostatin receptor based PET/CT –Somatostatin receptor based SPECT/CT - Neuro Endocrine Tumors (NET)

Introduction

Among the in vivo imaging modalities, diagnostic nuclear medicine has the major advantage providing a functional and/or biological approach. The radiopharmaceutical is administered at minute amounts that induce no adverse effect but results in a radiation exposure to the patient and also to the hospital staff, the accompanying persons and the general public in the close vicinity of the patient during the hours following imaging. Patients are released from the nuclear medicine department after image acquisition when the uptake of the radiopharmaceutical by the target organs or lesions is rapid enough. For some other examinations with a long uptake phase of the radiopharmaceutical by the target lesions, the patient leaves the department just after administration, and comes back for image acquisition.

There is currently a growing concern of the public about radiation exposure. In order to address this concern on the basis of actual measurements, we performed a bibliographic survey about the equivalent dose rate at 1 m (EDR-1m) of a patient who has been administered a radiopharmaceutical, at the moment when he/she is exiting the nuclear medicine department. Very few data in this domain were actually published and there is a complete lack of data for the less frequently used or the most recently introduced radiopharmaceuticals. We have thus undertaken a survey by measuring the EDR-1m of patients exiting our nuclear medicine departments after being administered a radiopharmaceutical.

For logistical reasons, we decided to limit the measurements to patients who have been referred for diagnostic nuclear medicine imaging due to a neuroendocrine tumor (NET). This is not a very frequent condition, but functional imaging using nuclear medicine modalities plays a major role in the management of those patients who undergo nuclear medicine imaging in a large proportion [1]. The functional imaging of NET is

currently performed using the two main techniques of diagnostic nuclear medicine: positron emission tomography (PET) or tomoscintigraphy (SPECT) [2]. Several radiopharmaceuticals are available, which are selected on a patient-basis according to the aggressiveness and the primary location of the NET [3]. For PET imaging of NET [4, 5], the most frequently used radiopharmaceuticals are the glucose analogue ^{18}F-fluorodeoxyglucose (FDG), the aminoacid analogue ^{18}F-fluorodihydroxyphenylalanine (FDOPA) and a ^{68}Ga labeled ligand of somatostatin receptors, e.g. edotreotide (DOTATOC). For SPECT imaging of NET, the catecholamine analogue ^{123}I-metaiodobenzylguanidine (mIBG) and another ligand of somatostatin receptors ^{111}In-pentetrotide (PENT) have been used for decades [6]. Therefore nuclear imaging of NET has several specificities that we considered to be appropriate for our purpose: a reasonable sample of patients can represent the population of patients with NET who are referred to nuclear medicine imaging in a large proportion and several radiopharmaceuticals labeled with 4 different radionuclides are used with PET or SPECT, for which no or very little data on exposure rate from the patients are available.

Materials and methods

Patients and radiopharmaceuticals

The EDR-1m measurements were performed on all the consecutive patients referred to us for nuclear medicine imaging of a proven or suspected NET who gave their written consent allowing the use of their anonymized data for research purposes. PET/CTs with ^{68}Ga-DOTATOC, ^{18}F-FDOPA or ^{18}F-FDG were performed at hospital Tenon. SPECT/CTs with ^{111}In-pentreotide or ^{123}I-mIBG were performed at hospital Cochin. Prior to ^{123}I-mIBG imaging, patients underwent a thyroid blockade, precluding any

significant thyroid uptake that could interfere with the precocious sternal dose rate measurement.

In both centers, EDR-1m measurements were performed until the results of at least 10 patients were available for each of the radiopharmaceuticals. All the nuclear medicine examinations were performed according to the standard procedure of each department for each radiopharmaceutical (Table 1). The radiopharmaceuticals were registered and had a marketing authorization in France, except DOTATOC the use of which was authorized by the French medicine agency (ANSM) on an individual basis (autorisation temporaire d'utilisation nominative).

Dose rate detectors

The measurements were performed at Hôpital Tenon and Hôpital Cochin, using two different dose rate detectors, after their cross calibration had been done. The detector used at hospital Tenon was an identiFINDER N/9V (Aries). This gamma spectrometer is a Na I (Tl) scintillation detector**.** Its equivalent dose rate range includes the values expected in this study since it ranges from 0.01 µSv/h to 1 Sv/h. Besides, its energy range (15 keV to 3000 keV) includes the values of the main photonic rays of the radionuclides administered for NET imaging [7]: from 511 to 1883 keV for ^{68}Ga, 511 keV for ^{18} F, from 23 to 245 keV for ^{111}In and from 27 to 529 keV for ^{123}I .

The detector used at hospital Cochin was a PDS-100GN-ID Spectroscopic Pocket Radiation Detector that also matches all the same criteria. The difference between dose rates measured simultaneously with the two dectectors at 1m of a ^{51}Co source corresponding to the expected dose rate range was less than 0.1 µSv/h.

Timing of EDR-1m measurements

The equivalent dose rate was measured at a distance of 1 meter (EDR-1m) from the standing patient. In order to be the most accurate possible, a 1 meter stick was used to

define the distance between the patient and the detector. Two measurements were done with the detector facing 2 different anatomical landmarks: the sternum and the urinary bladder. The EDR-1m value was corrected from the background measured in the same room in the absence of patient; the typical background dose rate was 0.04-0.06 µSv/h. Our aim was to determine the EDR-1m when the patient is permitted to leave the nuclear medicine department: in case of multiple imaging sessions after one administration of the radiopharmaceutical, the measurements were only done before the patient exits the department for the first time.

Thus, for PET/CT examinations, the EDR-1m was measured after acquisition of images, approximately between 1.5 and 2 hours after the injection of the radiopharmaceutical. The patients voided before the acquisition of the PET images but rarely after, just before the measurements. For patients referred for SPECT, the measurements were performed a few minutes after the injection of the radiopharmaceutical, just before the patient leaves the nuclear medicine department since the acquisition of images is scheduled several hours later.

Statistics

Comparisons of EDR-1m according to the 5 radiopharmaceuticals were performed by analysis of variance (ANOVA). When the hypothesis of equality of variance was rejected using the Levene's test, ANOVA was replaced by the non-parametric Kruskal-Wallis test. The comparison between EDR-1m measurements facing the sternum and the urinary bladder was performed using the t test for paired values.

Results

The EDR-1m measurements were performed from April until October 2016, ending when data for at least ten patients were available for each radiopharmaceutical. A total of 103 paired measurements facing the sternum and the urinary bladder were performed in 98

patients, since 4 patients underwent several examinations: DOTATOC, FDG and PENT in one patient, DOTATOC and FDOPA in two patients, and PENT twice in the last one. As expected, the radiopharmaceutical differed according to the reason for referring the patient to nuclear imaging. Of the 53 DOTATOC PET/CTs, 19 were performed for staging or restaging of a pancreatic NET, 10 for staging or restaging of an intestinal or rectal NET, 6 for staging or restaging of a bronchial or thymic NET, 11 for characterization of a tumor suspicious for NET and 7 for a NET of unknown primary. Of the 15 FDOPA PET/CTs, 12 were performed for staging or restaging of a NET of the ileum, 2 for a NET of unknown primary and 1 for surveillance of a medullary thyroid cancer. Of the 13 FDG PET/CTs, 12 were performed for characterization of tumors, mainly lung nodules, potentially suspicious for a NET and 1 for surveillance of an atypical NET of the thymus. Of the 12 PENT SPECT/CTs, 4 were performed for staging or restaging of an intestinal NET, 2 for staging or restaging of a pancreatic NET, 3 for characterization of tumors potentially suspicious for a NET, 2 for a paraneoplastic Cushing syndrome and 1 for surveillance of an atypical NET of the thymus. Of the 10 mIBG SPECT/CT, 5 were performed for staging or restaging of a phaeochromocytoma, 4 for characterization of lesions suspicious for phaeochromocytoma and 1 for a paraneoplastic Cushing syndrome.

The main results of the study are reported in table 2. There was no significant difference in patients' characteristics (gender, age, body height, body weight, body mass index), according to the examination that was performed. The injected activity was significantly lower for DOTATOC than for all other radiopharmaceuticals. The standard deviation was smaller for SPECT tracers (PENT and mIBG), since the hospital Cochin team uses a "fixed activity" approach for those radiopharmaceuticals.

As expected, the time interval between injection and measurement immediately prior to patient departure was far shorter when the patient was referred for SPECT/CT (PENT or mIBG) than for PET/CT. For PET/CT, the patient stayed in the department after injection

until the nuclear medicine specialist checked his/her PET/CT images and allowed the patient to leave. The total stay in the department after injection was significantly shorter when DOTATOC was injected compared with the two fluorinated radiopharmaceuticals, although image acquisition could similarly be started 60 min after injection. This minimal delay was more closely observed for DOTATOC PET/CT than for fluorinated radiopharmaceuticals, probably due to the technical constraint related to the shorter physical half-life of ^{68}Ga.

One main result is that the equivalent dose rate at 1 m of the sternum or of the urinary bladder of patients injected with DOTATOC or mIBG was significantly lower than with any of the 3 other radiopharmaceuticals.

Comparing the EDR-1m measurements in the same patient facing the sternum and facing the urinary bladder, the latter was overall greater (paired t-test: $p<0.01$). Actually, there was a clear difference between the PET tracers that resulted in a higher EDR-1m facing the bladder ($n=81$, $p<0.001$) and the SPECT tracers that resulted in a non-significant trend to a lower EDR-1m facing the bladder ($n=22$, $p=0.07$).

As expected, there was a strong correlation between the EDR-1m and the injected activity (MBq or MBq/kg), all $r>0.5$, $p<0.001$. In order to test whether the lower EDR-1m with DOTATOC was a simple consequence of the significantly lower injected activity than that of other radiopharmaceuticals, we compared the EDR-1m divided by the injected activity (last two rows of table 2). Per unit of injected activity, the EDR-1m values were the lowest for mIBG, then for DOTATOC, with significantly lower EDR-1m values than those of PENT, its SPECT alternative. In contrast, we observed no significant correlation between EDR-1m and body mass index ($r=0.1$).

Discussion

The results of the present study show that the equivalent dose rate at 1m from the patient's sternum or bladder was less than 20 µSv/h for all patients when they left the nuclear medicine department, even though the highest values with FDOPA or FDG were close to that limit (table 2). Actually, there is no constraint threshold for this dose rate in EU or worldwide. Furthermore, the few different threshold values that were proposed concerned patients leaving a nuclear medicine department after radionuclide therapy, not a diagnostic procedure. The lowest and most recently proposed limit was 20 µSv/h [8]. In 2010, the practical rules of the Heads of the European Radiological protection Competent Authorities (HERCA) recommended a limit of 40 µSv/h [9].

When exiting the department of nuclear medicine, the NET patients injected with DOTATOC or mIBG on average delivered an EDR-1m of roughly a half of that of patients injected with other radiopharmaceuticals. For an injected activity of the same order of magnitude, the higher energy of the photons emitted by the PET radiopharmaceuticals was compensated by their shorter physical half-life, since the patient had a longer stay in the nuclear medicine department before exiting. This is a complementary argument for replacing SPECT by PET for imaging of the somatostatin receptor.

There were two major differences between PET and SPECT in the routine practice.

1) As revealed by SD values in table 2, a "fixed" activity was injected to patients referred for SPECT, according to the summary of product characteristics (SmPC) of those two radiopharmaceuticals (Table 1). In contrast, the injected activity of PET radiopharmaceuticals was more variable, depending on patient's body mass as recommended in their SmPC but also depending on logistical constraints: the delivered activity in the multidose vial for fluorinated radiopharmaceutical, and for ^{68}Ga-DOTATOC the eluted activity from the ^{68}Ge/^{68}Ga generator and the labeling yield.

2) The patients referred for SPECT left the department a few minutes after injection and came back for imaging, whereas the patients referred for PET left the department after imaging, at least one hour after injection (Table 2). This difference in the delay between injection and measurement explains why bladder EDR-1m was significantly greater than sternum EDR-1m with radiopharmaceuticals for PET but not for SPECT. As all five radiopharmaceuticals are excreted through the kidneys, the urinary excretion and the accumulation of the radiopharmaceutical in the bladder are just beginning when the patient exits the department after injection of those SPECT radiopharmaceuticals, whereas more than one hour after injection of a PET radiopharmaceutical the bladder has become a radiation source. In this context, the variability of individual biological half-lives between patients and the frequency of voiding enhance individual equivalent dose rate differences.

Both factors (homogeneous injected activity and more homogeneous and shorter delay after injection) explain why the EDR-1m values were much less widespread for SPECT radiopharmaceuticals compared to PET radiopharmaceuticals (table 2).

To the best of our knowledge derived from an extensive bibliographical survey, no data had so far been published concerning the EDR-1m at the time of patient departure from the nuclear medicine department after DOTATOC or FDOPA PET/CT. This lack of data enhances the interest of the present data for DOTATOC derived from a rather large patients sample (n= 53) representative of all indications in NET, with a growing demand. The sample size is more limited for FDOPA, but those data are probably the first of their kind. Very few data concerning FDG (Table 3), PENT (Table 4) or mIBG (Table 5) have been published. Overall, all series are in accordance with the fact that the patient may leave the nuclear medicine department according to the current practices, i.e. just after injection for ^{111}In-PENT or ^{123}I-MIBG, without risk of an excessive radiation exposure to the public. It is also clear that new developments in PET/CT scanners, particularly time

of flight (TOF) technology, has allowed a reduction in FDG injected activity and consequently reduced EDR-1m (Table 3). In contrast, Demir et al., who injected on average three times more FDG than us, reported EDR-1m measurements well above 20 µSv/h. Even when it was possible to normalize EDR-1m per MBq of injected activity, a rather large variation in results between studies with similar design can be observed. One possible explanation is the small number of patients in most studies, including ours apart from DOTATOC. Differences in individual functional processes leads to variability in EDR-1m enhanced by PET patients' longer stay in the department compared to SPECT patients. Nevertheless, this factor seems insufficient to explain a ratio of 3 in EDR-1m after PENT between the series of Kurtaran and ours: the waiting time is very short and the injected activities are not in the same proportion. A similar question can be raised when comparing the EDR-1m after mIBG which is significantly lower in the series of Ofluoglu et al. [15] compared to ours whereas the injected activity is almost twice greater. Alternative hypothesis involves the detectors themselves. Although our two detectors produced by two different manufacturers gave very close EDR-1m values, one cannot exclude that different dose rate detectors give discrepant results for the same measurements, particularly when the measurements have been performed over a period of 14 years or more.

Conclusion

When leaving the nuclear medicine department after ^{68}Ga DOTATOC PET/CT, the equivalent dose rate at 1m from the patient is lower than after ^{111}In-pentreotide injection, whereas it was higher after ^{18}F-FDOPA PET/CT than after ^{123}I-mIBG injection. Nevertheless, this dose rate was inferior to 20 µSv/h for all the 5 radiopharmaceuticals in all the patients. The current practice of our nuclear medicine departments in allowing the

patient to exit appears to be safe according to the radiation protection point of view. There is no need for restrictive advice for patients travelling by public or private transport when they are authorized to leave the department.

References

1. Kjaeer A, Knigge U. Use of radioactive substances in diagnosis and treatment of neuroendocrine tumors. Scand J Gastroenterol. 2015;50(6):740-7.

2. Baumann T, Rottenburger C, Nicolas G, Wild D. Gastroenteropancreatic neuroendocrine tumours (GEP-NET) - Imaging and staging. Best Pract Res Clin Endocrinol Metab. 2016; 30(1):45-57.

3. Montravers F, Grahek D, Kerrou K et al. Can fluorodihydroxyphenylalanine PET replace somatostatin receptor scintigraphy in patients with digestive endocrine tumors? *J Nucl Med*. 2006; 47 (9): 1455-62.

4. Balogova S, Talbot JN, Nataf V et al. 18F-fluorodihydroxyphenylalanine vs other radiopharmaceuticals for imaging neuroendocrine tumours according to their type. *Eur J Nucl Med Mol Imaging*. 2013;40(6):943-66.

5. Prasad V, Ambrosini V, Alavi A, Fanti S, Baum RP. PET/CT in neuroendocrine tumors: evaluation of receptor status and metabolism. PET Clin. 2008

6. Modlin IM, Tang LH. Approaches to the diagnosis of gut neuroendocrine tumors: the last word (today). Gastroenterology. 1997;112(2):583-90.

7. Delacroix D, Guerre JP, Leblanc P. Radionucléides et radioprotection. CEA Saclay. 3rd edition, 1998.

8. Calais PJ, Turner JH. Radiation safety of outpatient 177Lu-octreotate radiopeptide therapy of neuroendocrine tumors. Ann Nucl Med. 2014; 28(6):531-9.

9. HERCA. WGMA (sub group patient release). 131I therapy: patient release criteria. 2010. http://www.herca.org/uploaditems/documents/Annexe%20I_HERCA OH_2011_0005_HERCA_Release%20criteria%2030062010.pdf

10. Fayad E, Maia S, Zilnus A et al. Care continuity in post-scintigraphy period and radioactivity exposure of medical and technical staff. *Méd Nucl 2015; 39:380–5.*

11. Demir M, Demir B, Sayman H, Sager S, Sabbir Ahmed A, Uslu I. Radiation protection for accompanying person and radiation workers in PET/CT. Radiat Prot Dosimetry. 2011;147(4):528-32.

12. Cronin B, Marsden PK, O'Doherty MJ. Are restrictions to behaviour of patients required following fluorine-18 fluorodeoxyglucose positron emission tomographic studies? Eur J Nucl Med. 1999;26(2):121-8.

13. Morán V, Prieto E, García-García B et al. Radiation dose produced by patients during radiopharmaceutical incorporation in nuclear medicine diagnostic procedures. Rev Esp Med Nucl Imagen Mol. 2016;35(3):175-85.

14. Kurtaran A, Pfreitfellner J, Schaffarich P et al. Radiation doses deriving from patients undergoing 111In-DTPA-D-phe-1-octreotide scintigraphy. Eur J Nucl Med. 1997;24(10):1298-300.

15. Ofluoglu S, Preitfellner J, Fueger BJ et al. Radiation exposure around patients after administration of 123-MIBG. Nuklearmedizin. 2002;41(5):221-3.

Tables

Characteristics of radiopharmaceuticals	^{68}Ga-DOTATOC	^{18}F-FDOPA	^{18}F-FDG	^{111}In-pentetreotide	^{123}I-mIBG
Imaging modality and hospital of the nuclear medicine center	PET/CT Tenon	PET/CT Tenon	PET/CT Tenon	SPECT/CT Cochin	SPECT/CT Cochin
Radiopharmaceutical and producer	DOTATOC: Iason, Graz, Austria **&** ^{68}Ga: Galliapharm®, Eckert-Ziegler, Berlin, Germany	Iasodopa ®: Iason, Graz, Austria	Metatrace FDG ®: Siemens Healthcare, Frimley Camberley, UK ***or_*** Gluscan ®: AAA, St Genis-Pouilly, France	Octreoscan ®: Mallinckrodt Medical, Petten, The Netherlands	MIBG (^{123}I): Mallinckrodt Medical, Petten, The Netherlands ***or*** Adreview ®: GE Healthcare, Vélizy-Villacoublay, France
Physical half-life (min)	68	110	110	4032 (2.8 days)	792 (13.2 h)
Scheduled injected activity	1-2 MBq/kg BM	2.5-3.5 MBq/kg BM	2-3 MBq/kg BM	185 MBq	185 MBq
Scheduled time interval between injection and imaging (min)	45-90	10 (MTC) & 60	60-120	1440 (24h)	240 & 1440 (4 & 24h)
Photonic ray for imaging (keV)	511	511	511	245 & 171	159

Table 1: Radiopharmaceuticals and practical options at each center

BM: body mass, MTC: medullary thyroid cancer.

Characteristics & measurements / radiopharmaceutical	^{68}Ga-DOTATOC	^{18}F-FDOPA	^{18}F-FDG	^{111}In-pentetreotide (PENT)	^{123}I-mIBG	Comparison
Number of patients	53 (29 men, 24 women)	15 (6 men, 9 women)	13 (8 men, 5 women)	12 (6 men, 6 women)	10 (3 men, 7 women)	Khi-2: NSD in gender repartition
Age (years)	56.7 ± 12.3; 58 (30-76)	60.9 ± 12.1; 61 (29-78)	64.5 ± 17.0; 66 (37-89)	62.1 ± 12.6; 63 (38-81)	51.0 ± 10.2; 53 (30-65)	ANOVA: NSD
Body height (m)	1.70 ± 0.09; 1.71 (1.53-1.96)	1.70 ± 0.09; 1.67 (1.57-1.83)	1.66 ± 0.08; 1.69 (1.51-1.77)	1.70 ± 0.12; 1.72 (1.45-1.86)	1.68 ± 0.10; 1.69 (1.56-1.83)	ANOVA: NSD
Body mass (kg)	72.4 ± 13.8; 71 (49-105)	72.3 ± 13.5; 75 (50-91)	68.4 ± 20.6; 60 (39-120)	72.7 ± 13.7; 73.5 (54-95)	73.3 ± 11.0; 76.5 (58-88)	ANOVA: NSD
Body Mass Index ($kg.m^{-2}$)	24.9 ± 4.27; 24.5 (17.3-37.1)	24.6 ± 4.27; 24.4 (17.2-34.5)	24.6 ± 6.01; 23.9 (15.2-38.7)	25.1 ± 3.79; 24.4 (18.7-30.7)	26.3 ± 4.03; 25.3 (21.3-33.6)	ANOVA: NSD
Injected activity (MBq)	121 ± 23; 122 (80-170)	199 ± 48; 198 (97-262)	176 ± 56; 167 (98-321)	170 ± 7; 170 (158-179)	186 ± 5; 184 (176-194)	DOTATOC < all others KW: p<<0.001
Injected activity per body mass unit (MBq/kg)	1.72 ± 0.42; 1.77 (0.89-2.80)	2.74 ± 0.42; 2.83 (1.87-3.27)	2.59 ± 0.38; 2.51 (2.23-3.81)	2.41 ± 0.48; 2.30 (1.77-3.29)	2.58 ± 0.45; 2.43 (2.00-3.27)	DOTATOC < all others ANOVA: p<0.001
Time interval between injection and EDR-1m measurement	90 ± 16; 87 (66-126)	114 ± 14; 117 (86-130)	112 ± 39; 95 (82-220)	6.2 ± 3.5; 5 (2-15)	5.7 ± 2.6; 5 (3-10)	PENT & mIBG < DOTATOC < FDOPA & FDG

(min)						KW: p<<0.001
Equivalent dose rate at 1 m from the sternum (µSv/h)	4.73 ± 1.41; 4.75 (2.10-9.10)	9.76 ± 3.61; 9.50 (3.92-17.7)	9.34 ± 3.51; 8.80 (3.50-18.8)	9.56 ± 0.93; 9.43 (8.50-11.0)	4.94 ± 0.31; 4.89 (4.45-5.49)	DOTATOC & mIBG < all others KW: p<<0.001
Equivalent dose rate at 1 m from the bladder (µSv/h)	5.04 ± 1.37; 5.10 (2.13-8.20)	10.2 ± 3.20; 10.1 (4.57-15.8)	10.5 ± 4.28; 9.50 (3.80-21.2)	9.21 ± 1.31; 9.30 (5.81-11.2)	4.41 ± 0.93; 4.68 (2.80-5.65)	DOTATOC & mIBG < all others KW: p<<0.001
Equivalent dose rate at 1 m from the sternum per injected MBq (nSv/h/MBq)	39.4 ± 10.7; 37.7 (21.9-89.7)	51.7 ± 25.1; 45.5 (25.0-116)	54.4 ± 13.8; 57.1 (16.5-71.5)	56.3 ± 4.6; 55.5 (50-64)	26.6 ± 1.5 26.5 (23.6-29.5)	mIBG < DOTATOC & FDOPA < FDG & PENT KW: p<<0.001
Equivalent dose rate at 1 m from the bladder per injected MBq (nSv/h/MBq)	41.9 ± 10.0; 41.0 (25.4-88.5)	54.0 ± 23.0; 44.8 (26.1-104)	60.4 ± 15.5; 62.1 (17.9-82.9)	54.3 ± 7.3; 56.0 (34.1-62.5)	23.7 ± 4.9 25.0 (15.3-29.1)	mIBG < DOTATOC < FDOPA & PENT < FDG KW: p<<0.001

Table 2. Patients & imaging characteristics and equivalent dose rates at 1 m according to the radiopharmaceutical. Results are expressed as mean ± standard deviation; median (range). ANOVA: analysis of variance, KW: Kruskal-Wallis test, NSD: no significant difference.

^{18}F-FDG	Hôpital Tenon 2016 (present study)	Fayad E et al. 2015 [10]	Demir M et al. 2010 [11]	Cronin B et al. 1999 [12]
Number of patients	13	6	30	75
Injected activity (MBq)	176 ± 56; 167 (98-321)	241 ± 33 (130-311)	550	323 ; 297
Time between the injection and the EDR-1m measurement (min)	112 ± 39; 95	90	117 ± 11	113 ; 116
Dose rate detector	identiFINDER N/9V	AT 1123 APVL	Eberline ESP-2	series 1000 Mini-Instruments
Equivalent dose rate at 1 m from the sternum (µSv/h)	9.34 ± 3.51; 8.80 (3.50-18.8)	6.83 ± 1.58	50	14.7; 14 (3.5-32)
Equivalent dose rate at 1 m from the sternum per injected MBq (nSv/h/MBq)	54.4 ± 13.8; 57.1 (16.5-71.5)	NA	90	47; 43 (13-120)

Table 3. Studies reporting measurement of EDR-1m after injection of ^{18}F-FDG. Mean ± SD; median (range).

^{111}In-pentetreotide	Hôpital Cochin 2016 (present study)	Fayad E et al. 2015 [10]	Moràn V et al. 2016 [13]	Kurtaran et al 1997 [14]
Number of patients	12	6	2	16
Injected activity (MBq)	170 ± 7 (158-179)	119 ± 67 (105-128)	200-220	140 ± 40
Time between the injection and the EDR-1m measurement (min)	6.2 ± 5	15	230-240	10-20
Dose rate detector	PDS-100GN-ID	AT 1123 APVL	MiniTRACE Genitron Instruments	Berthold LB 133
Equivalent dose rate at 1 m from the sternum (µSv/h)	9.56 ± 0.93; 9.43 (8.50-11.0)	5.5 ± 0.51	9.5	2.86 ± 1.22
Equivalent dose rate at 1 m from the sternum per injected MBq (nSv/h/MBq)	54.3 ± 7.3	NA	43	NA

Table 4. Studies reporting measurement of EDR-1m after injection of ^{111}In-pentetreotide.

Mean ± SD; median (range).

^{123}I-MIBG	Hôpital Cochin 2016 (present study)	Ofluoglu S et al. 2002 [15]
Number of patients	10	16
Average activity injected (MBq)	186 ± 5	340 ± 30
Time between the injection and the EDR-1m measurement (min)	5.7 ± 2.6	10
Dose rate detector	PDS-100GN-ID	Berthold LB 133
Equivalent dose rate at 1 m from the patient (µSv/h)	sternum: 4.94 ± 0.31 bladder: 4.41 ± 0.93	3.7 ± 0.7

Table 5. Studies reporting measurement of EDR-1m after injection of ^{123}I-mIBG. Mean ± SD; median (range).